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Correlation between the Microscopic and Macroscopic Effects of Microbeam Radiation Therapy (MRT) on the rat skin

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Beamline(s): X17B1

Introduction: In our previous microbeam radiation therapy (MRT) experiments on the normal rat skin model it was observed that the dose-response curve for the production of moist desquamation on the skin is very broad compared to the similar curve obtained with broad-beam irradiations. Furthermore, the microbeam dose at the onset of producing hair loss was much smaller (by at least 300 Gy) than onset dose for the induction of moist desquamation. A gradual augmentation of both these skin responses was recorded as the dose was increased. The present study was designed to explore the correlation between the microscopic effects observed in histological examinations and the macroscopic effects described above in the early stages of the damage. The comparison may provide clues on the biological basis of the normal tissue sparing effect of MRT.

Methods and Materials: Normal fisher 344 rats were irradiated on the external side of their thigh with arrays of vertical microbeams of 90 μm beam width and 300 μm center-to-center beam spacing from the X17B1 beamline. The skin surface of the external side of the thigh was positioned vertical to the beam during irradiations. Four groups of 3-4 rats in each were irradiated with The doses administered are 875, 1050, 1230 and 1400 Gys, respectively to provide increasing severity of the response. The skin responses of the Rats were followed up twice a day. Rats showing representative responses, in terms of hair clumping (HC) which is a response relating both to hair loss and moist desquamation, were euthanized at various time points (between days 11 to 17). Histological procedures are the same as described in previous experiments [1].

Results: At Day 11, when the differences in the severity of damage from different doses was clear, rats from each dose group were euthanized for skin histology. The macroscopic damage index was chosen to be HC; the HC scores found to be: visible HC for 875 Gy), minor HC for 1050 Gy, medium HC for 1230 Gy, and severe HC for 1400 Gy. From our earlier work we know that the epidermis starts to regenerate between days 6 to12 post-irradiation [1]. On the microscopic side, we found that as the administered dose increased the average thickness of regenerated epidermis and the count /size of regenerated islands decreased. In particular, at 875 Gy (Fig 1A) and 1050 Gy the regenerated epidermis is continuous, although its thickness varies depending on the density and size of regenerated colonies at different sites; at 1230 Gy the epidermis is continuous in most area. There are some scattered sites covered with a very thin layer of corny material, and small focal lesions depleted of epidermis, usually underneath an acellulous crust. At 1400 Gy most skin surface was depleted of epidermis and covered only with a large fused acellulous crust, with scattered sites of regenerated epidermis colonies underneath the crust. It appears that visible or minor hair-clumping may be attributed to the damage of hair follicles, while medium or severe hair clumping represent serum leakage response due to focal or larger lesions of epidermis depletion which are covered soon after their appearance by first epidermis regeneration and the crust formation. For the rats euthanized at Day 12, in the 875 Gy group, the only change from Day 11 was some further hair loss; in contrast, in the 1050 Gy and 1230 Gy groups, beside additional hair loss the hair clumping was increased to the next level, which was confirmed microscopically similar to the reactions observed for comparable macroscopic levels seen in Day 11. One rat from each of the latter two groups showed typical gross moist desquamation involving < 10% of the irradiated area up to Day 14; no further advance of skin damage was observed in those rats kept for longer term observation. One rat of 1230 Gy group, euthanized at Day 14, and another one of 1400 Gy group, euthanized at Day 17, both grossly scored as “crust formation”, were examined for histology (Fig 1B). In both cases, multiple small focal lesions depleted of epidermis were found underneath a single large acellulous crust, leaving most of the area covered with continuous epidermis. By Day 17 all rats from the 1400 Gy group showed typical moist desquamation involving 30-40% of the irradiated field, which lasted about 3 days and was microscopically characterized by a skin surface completely depleted of epidermis underneath high density fallen off-hair mixed with other acellulous, amorphous components.

Conclusions: The level of rat epidermis recovery under microscopy after microbeam irradiation is well correlated with our macroscopic scoring. The rat epidermis is capable of recovering quickly from damage produced by very high doses of microbeams through clonogenic proliferation followed by re-epithelialization.

References: 1. N. Zhong, G. Morris, T. Bacarian, Z. Hiz, M. Kershaw, P. Recksiek, L. Rigon, B. Scharf, R. Yakupov, and A. Dilmanian (2001) Histopathology of Normal Rat Skin after Irradiation with Arrays of Microplanar X-ray Beams. *NSLS Activity Report 2000*.

Fig 1: Microphotography of rat skin responses to microbeam irradiation. A, 875 Gy at Day 11 post-irradiation, significant colony formation and epidermis regeneration. B, 1230 Gy at Day 14 post-irradiation, as pointed by the arrow, microscopy lesions (epidermis depletion) were found, accompanied by active regeneration of epidermis.